AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application.

Listing of Claims:

1-5 (Cancelled)

6. (Currently Amended) A method for detecting an increased risk of developing Down's Syndrome ~~cardiovascular disease, or cancer~~ in a mammalian embryo or fetus, said method comprising detecting the presence of a polymorphic methionine synthase reductase (MTRR) in said embryo or fetus, ~~a test subject, wherein said test subject is said embryo or fetus~~ or in a future female parent of said embryo or said fetus, ~~and~~ wherein detection of a homozygous MTRR polymorphism in said future female parent, said embryo, or said fetus~~, or detection of either a homozygous or heterozygous MTRR polymorphism in both future parents~~ indicates an increased risk of developing ~~said neural tube defect,~~ Down's Syndrome~~, or cardiovascular disease~~ in said embryo or said fetus, wherein said polymorphism comprises a G instead of an A at position 66 relative to the first nucleotide of the start codon of MTRR.

7. (Currently Amended) The method of claim 6, wherein said polymorphic MTRR is detected by analyzing nucleic acid from said future female parent, said embryo, or said fetus ~~test subject~~.

8. (Original) The method of claim 7, wherein said nucleic acid is genomic DNA.

9. (Original) The method of claim 7, wherein said nucleic acid is cDNA.

10. (Cancelled)

11. (Currently Amended) The method of claim 7, wherein said polymorphic MTRR is detected by a method ~~further~~ comprising:

a) PCR-amplifying a segment of MTRR nucleic acid from said future female parent, said embryo, or said fetus using primers MSG108S (SEQ ID NO: 49) and AD292 (SEQ ID NO: 50), and

b) digesting the product of the PCR amplification reaction with the restriction enzyme *Nde* I, wherein a PCR product that is digested by *Nde* I indicates the presence of said polymorphic MTRR ~~an increased risk of developing a neural tube defect in a mammalian embryo or fetus~~.

12. (Withdrawn) The method of claim 6, wherein said polymorphic MTRR is detected by analyzing MTRR polypeptide from said test subject.

13. (Currently Amended) The method of claim 6, wherein said method comprises detecting the presence of said polymorphic MTRR in said future female parent ~~test subject is a~~

~~future female parent of said embryo or said fetus~~.

14. (Currently Amended) The method of claim 6, wherein said method comprises detecting the presence of said polymorphic MTRR in said embryo or fetus ~~test subject is said embryo or said fetus~~.

15. (Withdrawn) The method of claim 6, said method further comprising detecting the presence of a polymorphic methylenetetrahydrofolate reductase (MTHFR) in a test subject, wherein detection of said polymorphic MTHFR indicates an increased risk of developing said neural tube defect, Down's Syndrome, or cardiovascular disease in said embryo or said fetus.

16. (Withdrawn) The method of claim 15, wherein said polymorphic MTHFR has a T instead of a C at a nucleotide position equivalent to position 677 of SEQ ID NO: 51.

17. (Withdrawn) The method of claim 15, wherein said polymorphic MTHFR is detected by analyzing nucleic acid from said test subject.

18. (Withdrawn) The method of claim 15, wherein said polymorphic MTHFR is detected by analyzing polypeptide from said test subject.

19. (Withdrawn) The method of claim 6, said method further comprising measuring the

level of cobalamin in said test subject, wherein a low cobalamin level indicates an increased risk of developing said neural tube, cardiovascular disease or Down's Syndrome defect in said embryo or said fetus.

20. (Withdrawn) The method of claim 6, wherein said polymorphic MTRR contains a methionine instead of an isoleucine at amino acid position 22.

21-34 (Cancelled)

35. (Currently Amended) A method for detecting an increased risk of ~~Down's Syndrome,~~ cardiovascular disease~~, or cancer~~ in a mammal, said method comprising detecting the presence of a homozygous methionine synthase reductase (MTRR) polymorphism ~~that indicates an increased risk of Down's Syndrome, cardiovascular disease, or cancer~~ in said mammal, wherein said MTRR polymorphism comprises a G instead of an A at position 66 relative to the first nucleotide of the start codon of MTRR.

36. (Currently Amended) The method of claim 6, wherein said future female parent ~~test subject~~ is human.

37. (Previously Presented) The method of claim 35, wherein said mammal is human.

38-41 (Cancelled)

42. (Currently Amended) The method of claim 35, wherein said ~~polymorphic~~ MTRR polymorphism is detected by analyzing nucleic acid from said mammal.

43. (Previously Presented) The method of claim 35, wherein said cardiovascular disease is premature coronary artery disease.

44. (Cancelled)

45. (Withdrawn) A method for detecting an increased risk of a folate/cobalamin metabolic disorder in a mammal, said method comprising detecting the presence of a homozygous MTRR polymorphism that indicates an increased risk of a folate/cobalamin metabolic disorder in said mammal, wherein said polymorphism comprises

(a) a G instead of an A at position 66 relative to the first nucleotide of the start codon of MTRR,

(b) a deletion of 4 nucleotides starting from position 1675 (nucleotides 1675-1678) relative to the first nucleotide of the start codon of MTRR, or

(c) a deletion of 3 nucleotides starting from nucleotide 1726 (nucleotides 1726-1728) relative to the first nucleotide of the start codon of MTRR.

46. (Withdrawn) The method of claim 45, wherein said folate/cobalamin metabolic disorder is megablastic anemia, developmental delay, hyperhomocysteinuria, or hypomethionemia.

47. (Withdrawn) The method of claim 45, wherein said mammal is human.

48. (Withdrawn) The method of claim 45, further comprising measuring the level of cobalamin in said mammal.

49. (Withdrawn) The method of claim 45, wherein said polymorphic MTRR is detected by analyzing nucleic acid from said mammal.

50. (Currently Amended) A method for detecting an increased risk of developing a neural tube defect in a mammalian embryo or fetus, said method comprising detecting the presence of a homozygous methionine synthase reductase (MTRR) polymorphism ~~polymorphic methionine synthase reductase (MTRR)~~ and low serum cobalamin level in a ~~test subject, wherein said test subject is said embryo or fetus or a~~ future female parent of said embryo or ~~said~~ fetus, ~~and wherein detection of a homozygous MTRR polymorphism in said future parent, said embryo, or said fetus, or detection of either a homozygous or heterozygous MTRR polymorphism in both future parents indicates an increased risk of developing said neural tube defect in said embryo or said fetus,~~ wherein said MTRR polymorphism comprises a G instead of an A at position 66

relative to the first nucleotide of the start codon of MTRR.

51. (Currently Amended) The method of claim 50, wherein said future female parent ~~test subject~~ is human.

52. (Currently Amended) The method of claim 50, wherein said MTRR polymorphism ~~polymorphic MTRR~~ is detected by analyzing nucleic acid from said future female parent ~~test subject~~.

53. (Previously Presented) The method of claim 50, wherein said neural tube defect is spina bifida.

54. (Currently Amended) The method of claim 50, wherein detecting said low serum cobalamin level comprises detecting a concentration of serum cobalamin that is less than 328 pmol/L in said fetus or embryo, or a concentration of serum cobalamin that is less than 259 pmol/L in said future female parent of said embryo or fetus.

55. (New) A method for detecting an increased risk of developing a neural tube defect in a mammalian embryo or fetus, said method comprising detecting the presence of a homozygous methionine synthase reductase (MTRR) polymorphism and a homozygous methylenetetrahydrofolate reductase (MTHFR) polymorphism in said embryo or fetus, or in a future female parent of said embryo or fetus, wherein said MTRR polymorphism comprises a G

instead of an A at position 66 relative to the first nucleotide of the start codon of MTRR and said MTHFR polymorphism comprises a T instead of a C at position 677 relative to the first nucleotide of the start codon of MTHFR, wherein detection of said MTRR and MTHFR polymorphisms indicate an increased risk of developing said neural tube defect in said embryo or fetus.

56. (New) The method of claim 55, wherein said embryo or fetus is human.

57. (New) The method of claim 55, wherein said future female parent is human.

58. (New) The method of claim 55, wherein said MTRR and MTHFR polymorphisms are detected by analyzing nucleic acid from said embryo or fetus.

59. (New) The method of claim 55, wherein said neural tube defect is spina bifida.